

Supplementary S1 Material to:

“Thalassemia in the United Arab Emirates: Why It Can Be Prevented but Not Eradicated”

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I. Mathematical Model

The variables and the parameters are given as follows:

Variables

- (v1) G_M and G_F are boys and girls (children) under the age of twenty;
- (v2) S_M and S_F are the single male and female classes, and C_M and C_F are the single male and female carrier classes. These classes are populations at or over the age of twenty who can be called young adults;
- (v3) S_M^A and S_F^A are the marriageable single male and female classes, C_M^A and C_F^A are the marriageable single carrier male and female classes;
- (v4) U is the married (or united) class, and T_M and T_F are the male and female thalassemia major classes;
- (v5) S_K and S_K^{AE} are uneducated/educated K populations, respectively for $K = M$ or F ;
- (v6) S_M^{AE} , S_F^{AE} , C_M^{AE} , and C_F^{AE} are educated marriageable male and female singles and carrier populations;
- (v7) $N_M = S_M + S_M^E + S_M^{AE} + C_M^E + C_M^{AE}$ and $N_F = S_F + S_F^E + S_F^{AE} + C_F^E + C_F^{AE}$ are denoted as the total adult male and female populations, respectively;

Parameters

- (p1) α_M and α_F are marriage rates of male and female;

- (p2) α_s^M and α_s^F are the premarital screening rates of single male and female;
- (p3) η_T^M and η_T^F are the rates of being diagnosed as thalassemia major of male and female, respectively;
- (p4) η_C^M and η_C^F are the rates of being identified as thalassemia carrier of male and female, respectively;
- (p5) d_M and d_F are the natural death rates of male and female, and d_T is thalassemia induced death rate;
- (p6) b_M and b_F are the birth rates of boys and girls, respectively;
- (p7) γ_M and γ_F are the proportions of children becoming young adults;
- (p8) ν_M and ν_F are the marriage reconsideration rates of uneducated male and female carrier populations;
- (p9) ε is a proportion of educating marriageable single populations;
- (p10) $\tilde{\nu}_M$ and $\tilde{\nu}_F$ are marriage reconsideration rates of educated male and female carrier populations;
- (p11) d_M^G and d_F^G are child mortality rates.

Then, the full scope of the mathematical model for the thalassemia dynamics with the premarital and education factor is given by

$$\frac{dG_M}{dt} = b_M U - \zeta \eta_T^M G_M - (1 - \zeta \eta_T^M) \gamma_M G_M - d_M^G G_M \quad (1)$$

$$\frac{dG_F}{dt} = b_F U - \zeta \eta_T^F G_F - (1 - \zeta \eta_T^F) \gamma_F G_F - d_F^G G_F \quad (2)$$

$$\frac{dT_M}{dt} = \zeta \eta_T^M G_M - \left(\frac{\varepsilon(1 - \zeta \eta_T^M) \gamma_M G_M}{\gamma_M G_M + \gamma_F G_F} \right) T_M - d_T T_M \quad (3)$$

$$\frac{dT_F}{dt} = \zeta \eta_T^F G_F - \left(\frac{\varepsilon(1 - \zeta \eta_T^F) \gamma_F G_F}{\gamma_M G_M + \gamma_F G_F} \right) T_F - d_T T_F \quad (4)$$

$$\frac{dS_M}{dt} = (1 - \varepsilon)(1 - \zeta \eta_T^M) \gamma_M G_M - \alpha_s^M S_M - d_M S_M \quad (5)$$

$$\frac{dS_M^E}{dt} = \varepsilon(1 - \zeta \eta_T^M) \gamma_M G_M - \alpha_s^M S_M^E - d_M S_M^E \quad (6)$$

$$\frac{dS_M^{AE}}{dt} = (1 - \eta_C^M) \alpha_s^M S_M^E - \alpha_M S_M^{AE} \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A} - d_M S_M^{AE} \quad (7)$$

$$\frac{dC_M^{AE}}{dt} = \eta_C^M \alpha_s^M S_M^E - \alpha_M C_M^{AE} \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A} \quad (8)$$

$$+ \tilde{\nu}_M \alpha_M C_M^{AE} \frac{(C_F^A + C_F^{AE})}{N^A} - d_M C_M^{AE} \quad (9)$$

$$\frac{dS_M^A}{dt} = (1 - \eta_C^M) \alpha_s^M S_M - \alpha_M S_M^A \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A} - d_M S_M^A \quad (10)$$

$$\frac{dC_M^A}{dt} = \eta_C^M \alpha_s^M S_M - \alpha_M C_M^A \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A} \quad (11)$$

$$+ \nu_M \alpha_M C_M^A \frac{(C_F^A + C_F^{AE})}{N^A} - d_M C_M^A \quad (12)$$

$$\frac{dS_F}{dt} = (1 - \varepsilon)(1 - \zeta\eta_T^F)\gamma_F G_F - \alpha_s^F S_F - d_F S_F \quad (13)$$

$$\frac{dS_F^E}{dt} = \varepsilon(1 - \zeta\eta_T^F)\gamma_F G_F - \alpha_s^F S_F^E - d_F S_F^E \quad (14)$$

$$\frac{dS_F^{AE}}{dt} = (1 - \eta_C^F)\alpha_s^F S_F^E - \alpha_F S_F^{AE} \frac{(S_M^{AE} + C_M^{AE} + S_M^A + C_M^A)}{N^A} - d_F S_F^{AE} \quad (15)$$

$$\frac{dC_F^{AE}}{dt} = \eta_C^F \alpha_s^F S_F^E - \alpha_F C_F^{AE} \frac{(S_M^{AE} + C_M^{AE} + S_M^A + C_M^A)}{N^A} \quad (16)$$

$$+ \tilde{\nu}_F \alpha_F C_F^{AE} \frac{(C_M^A + C_M^{AE})}{N^A} - d_F C_F^{AE} \quad (17)$$

$$\frac{dS_F^A}{dt} = (1 - \eta_C^F)\alpha_s^F S_F - \alpha_F S_F^A \frac{(S_M^{AE} + C_M^{AE} + S_M^A + C_M^A)}{N^A} - d_F S_F^A \quad (18)$$

$$\frac{dC_F^A}{dt} = \eta_C^F \alpha_s^F S_F - \alpha_F C_F^A \frac{(S_M^{AE} + C_M^{AE} + S_M^A + C_M^A)}{N^A} \quad (19)$$

$$+ \nu_F \alpha_F C_F^A \frac{(C_M^A + C_M^{AE})}{N^A} - d_F C_F^A \quad (20)$$

$$\frac{dU}{dt} = \alpha_M (S_M^{AE} + C_M^{AE} + S_M^A + C_M^A) \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A} \quad (21)$$

$$+ \alpha_F (S_F^{AE} + C_F^{AE} + S_F^A + C_F^A) \frac{(S_M^{AE} + C_M^{AE} + S_M^A + C_M^A)}{N^A} \quad (22)$$

$$- \tilde{\nu}_M \alpha_M C_M^{AE} \frac{(C_F^A + C_F^{AE})}{N^A} - \nu_M \alpha_M C_M^A \frac{(C_F^A + C_F^{AE})}{N^A} \quad (23)$$

$$- \tilde{\nu}_F \alpha_F C_F^{AE} \frac{(C_M^A + C_M^{AE})}{N^A} - \nu_F \alpha_F C_F^A \frac{(C_M^A + C_M^{AE})}{N^A} - \frac{1}{2}(d_M + d_F)U, \quad (24)$$

where

$$\begin{aligned} \zeta = \frac{1}{U} & \left(\alpha_M (1 - \tilde{\nu}_M) C_M^{AE} \frac{(C_F^{AE} + C_F^A)}{N^A} + \alpha_M (1 - \nu_M) C_M^A \frac{(C_F^{AE} + C_F^A)}{N^A} \right. \\ & \left. + \alpha_F (1 - \tilde{\nu}_F) C_F^{AE} \frac{(C_M^{AE} + C_M^A)}{N^A} + \alpha_F (1 - \nu_F) C_F^A \frac{(C_M^{AE} + C_M^A)}{N^A} \right) \end{aligned}$$

is the proportion of carrier-carrier marriages without marriage reconsideration even with the education and premarital screening.

We provide the details of the model equations in (1) to (24) as follows: Note that all female population will have the similar features as the male population presented here, hence we omit the explanation about the female classes.

- Children Classes (G_M and G_F)

In Eqs. (1) and (2), $b_M U$ and $b_F U$ are birth of boys and girls, $\zeta \eta_T^M G_M$ and $\zeta \eta_T^F G_F$ are diagnosed thalassemia populations proportional to the carrier-carrier marriages.

$(1 - \zeta \eta_T^M) \gamma_M G_M$ and $(1 - \zeta \eta_T^F) \gamma_F G_F$ are non thalassemia children who become young adults at the age of twenty years old, and $d_M^G G_M$ and $d_F^G G_F$ are death of the children populations.

- Thalassemia Classes (T_M and T_F)

In Eqs. (3) and (4), $\zeta \eta_T^M G_M$ and $\zeta \eta_T^F G_F$ are diagnosed thalassemia populations and $d_T T_M$ is the death of thalassemia population due to the illness.

$-\left(\frac{\varepsilon(1 - \zeta \eta_T^M) \gamma_M G_M}{\gamma_M G_M + \gamma_F G_F}\right) T_M$ and $-\left(\frac{\varepsilon(1 - \zeta \eta_T^F) \gamma_F G_F}{\gamma_M G_M + \gamma_F G_F}\right) T_F$ are the reduction of thalassemia populations due to the education of non-thalassemia young adults on thalassemia.

- Single non-educated and educated male classes (S_M and S_M^E)

In Eqs. (5) and (6), $(1 - \varepsilon)(1 - \zeta \eta_T^M) \gamma_M G_M$ are non-educated single males who are non-thalassemia and young adults, and $\varepsilon(1 - \zeta \eta_T^M) \gamma_M G_M$ are educated single males who are non-thalassemia young adults. $\alpha_s^M S_M$ and $\alpha_s^M S_M^E$ are populations who take the premarital screening when they are about to marry. $d_M S_M$ and $d_M S_{EM}$ are death of the two classes, respectively.

- Single educated marriageable male class (S_M^{AE})

In Eq. (7), $(1 - \eta_C^M) \alpha_s^M S_M^E$ is the normal and non-carrier population screened from the educated single male population, and $\alpha_M S_M^{AE} \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A}$ is the marrying population who will be flushed to the married class U . $d_M S_M^{AE}$ is the death of this class.

- Carrier (single) educated marriageable male class (C_M^{AE})

In Eqs. (8) and (9), $\eta_C^M \alpha_s^M S_M^E$ is the carrier population screened from the educated single male population, and $\alpha_M C_M^{AE} \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A}$ is the marrying carrier population who will be flushed to the married class U . $\tilde{\nu}_M \alpha_M C_M^{AE} \frac{(C_F^A + C_F^{AE})}{N^A}$ is the

proportion of the educated carrier males who **decide not to marry carrier females**. This is the proportion of reconsideration of marriage of carrier male population who have been educated on thalassemia. $d_M C_M^{AE}$ is the death of this class.

- Single and carrier (single) marriageable who are NOT educated on thalassemia (S_M^A and C_M^A)

In Eqs. (10) and (11), $(1 - \eta_C^M) \alpha_s^M S_M$ and $\eta_C^M \alpha_s^M S_M$ are normal and carrier male populations screened from the non educated single male and carrier male populations. The marriages of these populations are $\alpha_M S_M^A \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A}$ and $\alpha_M C_M^A \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A}$, respectively. $d_M S_M^A$ and $d_M C_M^A$ are the deaths of these classes, respectively. In Eq. (12) $\nu_M \alpha_M C_M^A \frac{(C_F^A + C_F^{AE})}{N^A}$ is the proportion of the uneducated carrier males who **decide not to marry carrier females**. This is the proportion of reconsideration of marriage of carrier male population who have been screened and knows the consequence of the carrier-carrier marriage.

- Married (united) class (U)

In Eqs. (21) and (22), $\alpha_M (S_M^{AE} + C_M^{AE} + S_M^A + C_M^A) \frac{(S_F^{AE} + C_F^{AE} + S_F^A + C_F^A)}{N^A}$ and $\alpha_F (S_F^{AE} + C_F^{AE} + S_F^A + C_F^A) \frac{(S_M^{AE} + C_M^{AE} + S_M^A + C_M^A)}{N^A}$ are married males and females, respectively. In Eqs. (23) and (24), $\tilde{\nu}_M \alpha_M C_M^{AE} \frac{(C_F^A + C_F^{AE})}{N^A}$ and $\tilde{\nu}_F \alpha_F C_F^{AE} \frac{(C_M^A + C_M^{AE})}{N^A}$ are the proportion of carrier educated males and females who reconsider their carrier-carrier marriage, and $\nu_M \alpha_M C_M^A \frac{(C_F^A + C_F^{AE})}{N^A}$ and $\nu_F \alpha_F C_F^A \frac{(C_M^A + C_M^{AE})}{N^A}$ are that of carrier non-educated males and females who reconsider their carrier-carrier marriage. Finally, $\frac{(d_M + d_F)U}{2}$ is the death of this class.

II. Analysis of Model

Note that all variables remain nonnegative, i.e. $\frac{dH}{dt} > 0$ if $H = 0$, where $H = \{G_M, G_F, S_M, S_M^E, S_M^{AE}, C_M^{AE}, S_M^A, C_M^A, S_M, S_F^E, S_F^{AE}, C_F^{AE}, S_F^A, C_F^A, U\}$. Also,

$$\frac{dN}{dt} \leq (b_M + b_F)U - \bar{d}N \Rightarrow N(t) \leq \frac{b_M + b_F}{\bar{d}} \bar{U},$$

where $N = \sum_{K=M,F}(G_K + S_K^E + S_K^{AE} + C_K^{AE} + S_K^A + C_K^A) + U$, \bar{U} is the maximum number of married couples over a considered time span, and \bar{d} is the minimum of all death rates. Then, we consider two ideal situations that are represented by two equilibrium points, namely,

- (i) Type I: Thalassemia free equilibrium point, i.e., $T_M = T_F = 0$, $C_M = C_M^A = C_M^{AE} = 0$, and $C_F = C_F^A = C_F^{AE} = 0$;
- (ii) Type II: Thalassemia major free only equilibrium point, i.e., $T_M = T_F = 0$ only C_M , C_M^A , C_M^{AE} , C_F , C_F^A , C_F^{AE} are not necessarily zero

as time evolves in a long term. To investigate if (i) and (ii) are achievable via pre-marital screening and education factor, we will calculate two jacobian matrices which are obtained by differentiating each equation in eqs. (1) to (24) with seventeen variables in order $(G_M, G_F, T_M, T_F, S_M, S_M^E, S_M^{AE}, C_M^{AE}, S_M^A, C_M^A, S_F, S_F^E, S_F^{AE}, C_F^{AE}, S_F^A, C_F^A, U)$ and substituting the two equilibrium points in them.

Type I. Thalassemia free equilibrium point

$$(G_M^*, G_F^*, 0, 0, S_M^*, S_M^{AE*}, 0, S_M^{A*}, 0, S_F^*, S_F^{AE*}, 0, S_F^{A*}, 0, U^*)$$

For this equilibrium point, we obtain the following jacobian matrix J_1 :

$$\begin{bmatrix}
-a_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & b_M \\
0 & -b_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & b_F \\
0 & 0 & -c_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -d_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
e_1 & 0 & 0 & 0 & -e_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
f_1 & 0 & 0 & 0 & 0 & -f_6 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & g_6 & -B & D & D & D & 0 & 0 & -D & -D & -D & -D & 0 \\
0 & 0 & 0 & 0 & 0 & h_6 & 0 & -C & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & i_5 & 0 & E & E & -\tilde{B} & E & 0 & 0 & -E & -E & -E & -E & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -C & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & k_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -k_{11} & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & l_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -l_{12} & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & -H & -H & -H & -H & 0 & m_{12} & -F & H & H & H & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & n_{12} & 0 & -G & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & -I & -I & -I & -I & p_{11} & 0 & I & I & -\tilde{F} & I & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & q_{11} & 0 & 0 & 0 & 0 & -G & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & J & J & J & J & 0 & 0 & \tilde{J} & \tilde{J} & \tilde{J} & \tilde{J} & r_{17}
\end{bmatrix}, \quad (25)$$

where

- $a_1 = d_M^G + \gamma_M$, $b_2 = d_F^G + \gamma_F$, $c_3 = d_T + \frac{\varepsilon \gamma_M G_M^*}{\gamma_M G_M^* + \gamma_F G_F^*}$ and $d_4 = d_T + \frac{\varepsilon \gamma_F G_F^*}{\gamma_M G_M^* + \gamma_F G_F^*}$;
- $e_1 = \gamma_M(1 - \varepsilon)$ and $e_5 = \alpha_s^M + d_M$, and $f_1 = \varepsilon \gamma_M$ and $f_6 = \alpha_s^M + d_M$;
- $g_6 = \alpha_s^M(1 - \eta_M^C)$, $B = d_M + \alpha_M N_{AF}^* \frac{(N_A^* - S_M^{AE*})}{(N_A^*)^2}$ and $D = \frac{\alpha_M N_{AF}^* - S_M^{AE*}}{(N_A^*)^2}$, where $N_A^* = N_{AM}^* + N_{AF}^*$, $N_{AM}^* = S_M^{AE*} + S_M^{A*}$ and $N_{AF}^* = S_F^{AE*} + S_F^{A*}$;
- $h_6 = \alpha_s^M \eta_M^C$ and $C = d_M + \frac{\alpha_M N_{AF}^*}{N_A^*}$;
- $i_5 = \alpha_s^M$, $\tilde{B} = d_M + \alpha_M N_{AF}^* \frac{(N_A^* - S_M^{A*})}{(N_A^*)^2}$, and $E = \frac{\alpha_M N_{AF}^* S_M^{A*}}{(N_A^*)^2}$;
- $k_2 = \gamma_F(1 - \varepsilon)$ and $k_{11} = \alpha_s^F + d_F$, $l_2 = \varepsilon \gamma_F$ and $l_{12} = \alpha_s^F + d_F$;
- $m_{12} = \alpha_s^F(1 - \eta_F^C)$, $F = d_F + \alpha_F N_{AM}^* \frac{(N_A^* - S_F^{AE*})}{(N_A^*)^2}$, and $H = \frac{\alpha_F N_{AM}^* S_F^{AE*}}{(N_A^*)^2}$;

- $n_{12} = \alpha_s^F \eta_F^C$ and $G = d_F + \frac{\alpha_F N_{AM}^*}{N_A^*}$;
- $p_{11} = \alpha_s^F (1 - \eta_F^C)$, $\tilde{F} = d_F + \alpha_F N_{AM}^* \frac{(N_A^* - S_F^{A*})}{(N_A^*)^2}$, and $I = \frac{\alpha_F N_{AM}^* S_F^{A*}}{(N_A^*)^2}$;
- $q_{11} = \alpha_s^F \eta_F^C$, $r_{17} = -\frac{d_M + d_F}{2}$, $J = \frac{(\alpha_M + \alpha_F)(N_{AF}^*)^2}{(N_A^*)^2}$, and $\tilde{J} = \frac{(\alpha_M + \alpha_F)(N_{AM}^*)^2}{(N_A^*)^2}$.

Type II. Thalassemia major free only equilibrium point

$$(G_M^*, G_F^*, 0, 0, S_M^*, S_M^{AE*}, C_M^{AE*}, S_M^{A*}, C_M^{A*}, S_F^*, S_F^{AE*}, C_F^{AE*}, S_F^{A*}, C_F^{A*}, U^*)$$

For this equilibrium point we obtain the following jacobian matrix J_2 :

$$\begin{bmatrix} -a_1 & 0 & 0 & 0 & 0 & 0 & A & A_t & A & C_t & 0 & 0 & A & A'_t & A & C'_t & a_{17} \\ 0 & -b_2 & 0 & 0 & 0 & 0 & \tilde{A} & \tilde{A}_t & \tilde{A} & \tilde{C}_t & 0 & 0 & \tilde{A} & \tilde{A}'_t & \tilde{A} & \tilde{C}'_t & b_{17} \\ c_1 & 0 & -c_3 & 0 & 0 & 0 & -B & -B_t & -B & -D_t & 0 & 0 & -B & -B'_t & -B & -D'_t & c_{17} \\ 0 & d_2 & 0 & -d_4 & 0 & 0 & -\tilde{B} & -\tilde{B}_t & -\tilde{B} & -\tilde{D}_t & 0 & 0 & -\tilde{B} & -\tilde{B}'_t & -\tilde{B} & -\tilde{D}'_t & d_{17} \\ e_1 & 0 & 0 & 0 & -e_5 & 0 & E & E_t & E & F_t & 0 & 0 & E & E'_t & E & F'_t & -e_{17} \\ f_1 & 0 & 0 & 0 & 0 & -f_6 & \tilde{E} & \tilde{E}_t & \tilde{E} & \tilde{F}_t & 0 & 0 & \tilde{E} & \tilde{E}'_t & \tilde{E} & \tilde{F}'_t & -f_{17} \\ 0 & 0 & 0 & 0 & 0 & g_6 & -g_7 & G & G & G & 0 & 0 & -\tilde{M} & -\tilde{M} & -\tilde{M} & -\tilde{M} & 0 \\ 0 & 0 & 0 & 0 & 0 & h_6 & H & -h_8 & H & H & 0 & 0 & -\tilde{N} & -\tilde{P} & -\tilde{N} & -\tilde{P} & 0 \\ 0 & 0 & 0 & 0 & i_5 & 0 & I & I & -i_9 & I & 0 & 0 & -\tilde{Q} & -\tilde{Q} & -\tilde{Q} & -\tilde{Q} & 0 \\ 0 & 0 & 0 & 0 & j_5 & 0 & J & J & J & -j_{10} & 0 & 0 & -\tilde{R} & -\tilde{S} & -\tilde{R} & -\tilde{S} & 0 \\ 0 & k_2 & 0 & 0 & 0 & 0 & K & L_t & K & L & -k_{11} & 0 & K & L'_t & K & L' & -k_{17} \\ 0 & l_2 & 0 & 0 & 0 & 0 & \tilde{K} & \tilde{L}_t & \tilde{K} & \tilde{L} & 0 & -l_{12} & \tilde{K} & \tilde{L}'_t & \tilde{K} & \tilde{L}' & -l_{17} \\ 0 & 0 & 0 & 0 & 0 & 0 & -M & -M & -M & -M & 0 & m_{12} & -m_{13} & \tilde{G} & \tilde{G} & \tilde{G} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -N & -P & -N & -P & 0 & n_{12} & \tilde{H} & -n_{14} & \tilde{H} & \tilde{H} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -Q & -Q & -Q & -Q & p_{11} & 0 & \tilde{I} & \tilde{I} & -p_{15} & \tilde{I} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -R & -S & -R & -S & q_{11} & 0 & \tilde{J} & \tilde{J} & \tilde{J} & -q_{16} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & X & Y & X & Y & 0 & 0 & X & \tilde{Y} & X & \tilde{Y} & -r_{17} \end{bmatrix}, \quad (26)$$

where

- (i) $C_{Fadd} = (C_F^{A*} + C_F^{AE*})$ and $C_{Madd} = (C_M^{A*} + C_M^{AE*})$
 $C_{FaddnuM} = \alpha_M (C_F^{A*} + C_F^{AE*}) \{ (1 - \tilde{\nu}_M) C_M^{AE*} + (1 - \nu_M) C_M^{A*} \}$
 $C_{MaddnuF} = \alpha_F (C_M^{A*} + C_M^{AE*}) \{ (1 - \tilde{\nu}_F) C_F^{AE*} + (1 - \nu_F) C_F^{A*} \}$
 $N_{AF}^* = S_M^{AE*} + S_M^{A*} + C_M^{AE*} + C_M^{A*}$ and $N_{AM}^* = S_F^{AE*} + S_F^{A*} + C_F^{AE*} + C_F^{A*}$
 $N_A^* = N_{AF}^* + N_{AM}^*$;

$$\begin{aligned}
\text{(ii)} \quad Z_1 &= \frac{C_{FaddnuM} + C_{MaddnuF}}{N_A^*}; \\
\text{(iii)} \quad \tilde{Z}_2 &= \frac{\alpha_F((1 - \nu_F)C_F^{A*} + (1 - \tilde{\nu}_F)C_F^{AE*}) + \alpha_M(1 - \tilde{\nu}_M)C_{Fadd}}{N_A^*}; \\
\text{(iv)} \quad Z_2 &= \frac{\alpha_F((1 - \nu_F)C_F^{A*} + (1 - \tilde{\nu}_F)C_F^{AE*}) + \alpha_M(1 - \nu_M)C_{Fadd}}{N_A^*}; \\
\text{(v)} \quad \tilde{Z}_3 &= \frac{\alpha_M((1 - \nu_M)C_M^{A*} + (1 - \tilde{\nu}_M)C_M^{AE*}) + \alpha_F(1 - \tilde{\nu}_F)C_{Madd}}{N_A^*}; \\
\text{(vi)} \quad Z_3 &= \frac{\alpha_M((1 - \nu_M)C_M^{A*} + (1 - \tilde{\nu}_M)C_M^{AE*}) + \alpha_F(1 - \nu_F)C_{Madd}}{N_A^*};
\end{aligned}$$

- $a_1 = d_M^G + \gamma_M + \frac{(1 - \gamma_M)\eta_M^T Z_1}{U^*}$, $c_1 = \frac{\eta_M^T Z_1}{U^*}$, $e_1 = \gamma_M(1 - \varepsilon)(1 - \eta_M^T) \frac{Z_1}{U^*}$ and $f_1 = \gamma_M \varepsilon(1 - \eta_M^T) \frac{Z_1}{U^*}$;
- $b_2 = d_F^G + \gamma_F + \frac{(1 - \gamma_F)\eta_F^T Z_1}{U^*}$, $d_2 = \frac{\eta_F^T Z_1}{U^*}$, $k_2 = \gamma_F(1 - \varepsilon)(1 - \eta_F^T) \frac{Z_1}{U^*}$ and $l_2 = \gamma_F \varepsilon(1 - \eta_F^T) \frac{Z_1}{U^*}$;
- $c_3 = d_T + \frac{\varepsilon\gamma_M(1 - \eta_M^T)G_M Z_1}{(\gamma_F G_F + \gamma_M G_M)U^*}$ and $d_4 = d_T + \frac{\varepsilon\gamma_F(1 - \eta_F^T)G_F Z_1}{(\gamma_F G_F + \gamma_M G_M)U^*}$;
- $e_5 = f_6 = d_M + \alpha_s^M$, $i_5 = g_6 = \alpha_s^M(1 - \eta_M^T)$, and $j_5 = h_6 = \alpha_s^M \eta_M^T$;
- $g_7 = d_M + \frac{\alpha_M N_{AF}^*(N_A^* - S_M^{AE*})}{(N_A^*)^2}$ and $h_8 = d_M + \frac{\alpha_M(N_A^* - C_M^{AE*})(N_{AF}^* - \tilde{\nu}_M C_{Fadd})}{(N_A^*)^2}$,
 $i_9 = d_M + \frac{\alpha_M N_{AF}^*(N_A^* - S_M^{A*})}{(N_A^*)^2}$ and $j_{10} = d_M + \frac{\alpha_M(N_A^* - C_M^{A*})(N_{AF}^* - \nu_M C_{Fadd})}{(N_A^*)^2}$;
- $k_{11} = l_{12} = d_F + \alpha_s^F$, $p_{11} = m_{12} = \alpha_s^F(1 - \eta_F^C)$, and $q_{11} = n_{12} = \alpha_s^F \eta_F^C$;
- $m_{13} = d_F + \frac{\alpha_F N_{AM}^*(N_A^* - S_F^{AE*})}{(N_A^*)^2}$ and $n_{14} = d_F + \frac{\alpha_F(N_A^* - C_F^{AE*})(N_{AM}^* - \tilde{\nu}_F C_{Madd})}{(N_A^*)^2}$,
 $p_{15} = d_F + \frac{\alpha_F N_{AM}^*(N_A^* - S_F^{A*})}{(N_A^*)^2}$ and $q_{16} = d_F + \frac{\alpha_F(N_A^* - C_F^{A*})(N_{AM}^* - \nu_F C_{Madd})}{(N_A^*)^2}$;
- $a_{17} = b_M - \frac{(1 - \gamma_M)\eta_M^T G_M^* Z_1}{(U^*)^2}$ and $b_{17} = b_F - \frac{(1 - \gamma_F)\eta_F^T G_F^* Z_1}{(U^*)^2}$,
 $c_{17} = \frac{\eta_M^T G_M^* Z_1}{(U^*)^2}$ and $d_{17} = \frac{\eta_F^T G_F^* Z_1}{(U^*)^2}$,
 $e_{17} = \frac{(1 - \varepsilon)\eta_M^T \gamma_M G_M^* Z_1}{(U^*)^2}$ and $f_{17} = \frac{\varepsilon\eta_M^T \gamma_M G_M^* Z_1}{(U^*)^2}$,

$$k_{17} = \frac{(1 - \varepsilon)\eta_F^T \gamma_F G_F^* Z_1}{(U^*)^2} \text{ and } l_{17} = \frac{\varepsilon \eta_F^T \gamma_F G_F^* Z_1}{(U^*)^2},$$

$$r_{17} = \frac{d_M + d_F}{2};$$

- $A = \frac{(1 - \gamma_M)\eta_M^T G_M Z_1}{N_A^* U^*}$ and $\tilde{A} = \frac{(1 - \gamma_F)\eta_F^T G_F Z_1}{N_A^* U^*}$,
 $A_t = \frac{(1 - \gamma_M)\eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$ and $\tilde{A}_t = \frac{(1 - \gamma_F)\eta_F^T G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$,
 $A'_t = \frac{(1 - \gamma_M)\eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$ and $\tilde{A}'_t = \frac{(1 - \gamma_F)\eta_F^T G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$
 $C_t = \frac{(1 - \gamma_M)\eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_2)$ and $\tilde{C}_t = \frac{(1 - \gamma_F)\eta_F^T G_F}{N_A^* U^*} (Z_1 - Z_2)$,
 $C'_t = \frac{(1 - \gamma_M)\eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_3)$ and $\tilde{C}'_t = \frac{(1 - \gamma_F)\eta_F^T G_F}{N_A^* U^*} (Z_1 - Z_3)$;

- $B = \frac{\eta_M^T G_M Z_1}{N_A^* U^*}$ and $\tilde{B} = \frac{\eta_F^T G_F Z_1}{N_A^* U^*}$,
 $B_t = \frac{\eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$ and $\tilde{B}_t = \frac{\eta_F^T G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$,
 $B'_t = \frac{\eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$ and $\tilde{B}'_t = \frac{\eta_F^T G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$,
 $D_t = \frac{\eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_2)$ and $\tilde{D}_t = \frac{\eta_F^T G_F}{N_A^* U^*} (Z_1 - Z_2)$,
 $D'_t = \frac{\eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_3)$ and $\tilde{D}'_t = \frac{\eta_F^T G_F}{N_A^* U^*} (Z_1 - Z_3)$;

- $E = \frac{(1 - \varepsilon)\eta_M^T G_M Z_1}{N_A^* U^*}$, and $\tilde{E} = \frac{\varepsilon \eta_M^T G_M Z_1}{N_A^* U^*}$,
 $E_t = \frac{(1 - \varepsilon)\eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$ and $\tilde{E}_t = \frac{\varepsilon \eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$,
 $E'_t = \frac{(1 - \varepsilon)\eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$ and $\tilde{E}'_t = \frac{\varepsilon \eta_M^T G_M}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$,
 $F_t = \frac{(1 - \varepsilon)\eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_2)$ and $\tilde{F}_t = \frac{\varepsilon \eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_2)$,
 $F'_t = \frac{(1 - \varepsilon)\eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_3)$ and $\tilde{F}'_t = \frac{\varepsilon \eta_M^T G_M}{N_A^* U^*} (Z_1 - Z_3)$;

- $K = \frac{(1 - \varepsilon)\eta_F^T \gamma_F G_F Z_1}{N_A^* U^*}$, and $\tilde{K} = \frac{\varepsilon \eta_F^T \gamma_F G_F Z_1}{N_A^* U^*}$,
 $L_t = \frac{(1 - \varepsilon)\eta_F^T \gamma_F G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$ and $\tilde{L}_t = \frac{\varepsilon \eta_F^T \gamma_F G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_2)$,
 $L'_t = \frac{(1 - \varepsilon)\eta_F^T \gamma_F G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$ and $\tilde{L}'_t = \frac{\varepsilon \eta_F^T \gamma_F G_F}{N_A^* U^*} (Z_1 - \tilde{Z}_3)$,

$$\begin{aligned}
L &= \frac{(1-\varepsilon)\eta_F^T \gamma_F G_F}{N_A^* U^*} (Z_1 - Z_2) \text{ and } \tilde{L} = \frac{\varepsilon \eta_F^T \gamma_F G_F}{N_A^* U^*} (Z_1 - Z_2), \\
L' &= \frac{(1-\varepsilon)\gamma_F \eta_F^T G_F}{N_A^* U^*} (Z_1 - Z_3) \text{ and } \tilde{L}' = \frac{\varepsilon \eta_F^T \gamma_F G_F}{N_A^* U^*} (Z_1 - Z_3), \\
\bullet \quad G &= \frac{\alpha_M S_M^{AE*} N_{AF}^*}{(N_A^*)^2} \text{ and } \tilde{G} = \frac{\alpha_F S_F^{AE*} N_{AM}^*}{(N_A^*)^2}, \quad I = \frac{\alpha_M S_M^{A*} N_{AF}^*}{(N_A^*)^2} \text{ and } \tilde{I} = \frac{\alpha_F S_F^{A*} N_{AM}^*}{(N_A^*)^2}, \\
H &= \frac{\alpha_M C_M^{AE*} (N_{AF}^* - \tilde{\nu}_M C_{Fadd})}{(N_A^*)^2} \text{ and } \tilde{H} = \frac{\alpha_F C_F^{AE*} (N_{AM}^* - \tilde{\nu}_F C_{Madd})}{(N_A^*)^2}, \\
J &= \frac{\alpha_M C_M^{A*} (N_{AF}^* - \nu_M C_{Fadd})}{(N_A^*)^2} \text{ and } \tilde{J} = \frac{\alpha_F C_F^{A*} (N_{AM}^* - \nu_F C_{Madd})}{(N_A^*)^2}, \\
P &= \frac{\alpha_F C_F^{AE*} (N_{AF}^* - \tilde{\nu}_F (N_A^* - C_{Madd}))}{(N_A^*)^2} \text{ and } \tilde{P} = \frac{\alpha_M C_M^{AE*} (N_{AM}^* - \tilde{\nu}_M (N_A^* - C_{Fadd}))}{(N_A^*)^2}, \\
S &= \frac{\alpha_F C_F^{A*} (N_{AF}^* - \nu_F (N_A^* - C_{Madd}))}{(N_A^*)^2} \text{ and } \tilde{S} = \frac{\alpha_M C_M^{A*} (N_{AM}^* - \nu_M (N_A^* - C_{Fadd}))}{(N_A^*)^2}; \\
\bullet \quad M &= \frac{\alpha_F S_F^{AE*} N_{AF}^*}{(N_A^*)^2} \text{ and } \tilde{M} = \frac{\alpha_M S_M^{AE*} N_{AM}^*}{(N_A^*)^2}, \quad Q = \frac{\alpha_F S_F^{A*} N_{AF}^*}{(N_A^*)^2} \text{ and } \tilde{Q} = \frac{\alpha_M S_M^{A*} N_{AM}^*}{(N_A^*)^2}, \\
N &= \frac{\alpha_F C_F^{AE*} (N_{AF}^* + \tilde{\nu}_F C_{Madd})}{(N_A^*)^2} \text{ and } \tilde{N} = \frac{\alpha_M C_M^{AE*} (N_{AM}^* + \tilde{\nu}_M C_{Fadd})}{(N_A^*)^2}, \\
R &= \frac{\alpha_F C_F^{A*} (N_{AF}^* + \nu_F C_{Madd})}{(N_A^*)^2} \text{ and } \tilde{R} = \frac{\alpha_M C_M^{A*} (N_{AM}^* + \nu_M C_{Fadd})}{(N_A^*)^2}, \\
\bullet \quad X &= \frac{(\alpha_M + \alpha_F)(N_{AF}^*)^2}{(N_A^*)^2} \\
&\quad + \frac{\alpha_F C_{Madd}(\nu_F C_F^{A*} + \tilde{\nu}_F C_F^{AE*}) + \alpha_M C_{Fadd}(\nu_M C_M^{A*} + \tilde{\nu}_M C_M^{AE*})}{(N_A^*)^2}, \\
Y &= X - \frac{\alpha_F(\nu_F C_F^{A*} + \tilde{\nu}_F C_F^{AE*}) + \alpha_M \tilde{\nu}_M C_{Fadd}}{N_A^*}, \\
\tilde{Y} &= X - \frac{\alpha_M(\nu_M C_M^{A*} + \tilde{\nu}_M C_M^{AE*}) + \alpha_F \tilde{\nu}_F C_{Madd}}{N_A^*}.
\end{aligned}$$

Proposition 1 [1] [Chapter 6 Corollary 6.1.3] *The eigenvalues of $A = [m_{ij}]_{n \times n}$, an n by n matrix, are in the union of n discs*

$$\bigcup_{j=1}^n \{z \in \mathbb{C} : |z - a_{jj}| \leq C'_j(A)\}, \quad (27)$$

where \mathbb{C} is the set of complex numbers, a_{jj} are the diagonal entries in A , $\{z \in \mathbb{C} : |z - a_{jj}| \leq C'_j(A)\}$, is a disc in \mathbb{C} centered at a_{jj} with the radius $C'_j(A)$, and

$$C'_j(A) = \sum_{i \neq j} |a_{ij}|, \quad j = 1, \dots, n, \quad (28)$$

which is the absolute column sum without the the diagonal entry in the j^{th} column.

The above proposition is known as *Gersgorin disc theorem*. By using Proposition 1, we have the following result:

Theorem 2 *Type I equilibrium point, the thalassemia free equilibrium point*

$$(G_M^*, G_F^*, 0, 0, S_M^*, S_M^{AE*}, 0, S_M^{A*}, 0, S_F^*, S_F^{AE*}, 0, S_F^{A*}, 0, U^*),$$

and Type II equilibrium point, the thalassemia major free only equilibrium point

$$(G_M^*, G_F^*, 0, 0, S_M^*, S_M^{AE*}, C_M^{AE*}, S_M^{A*}, C_M^{A*}, S_F^*, S_F^{AE*}, C_F^{AE*}, S_F^{A*}, C_F^{A*}, U^*),$$

are unstable.

Proof From the jacobian matrix J_1 , we can calculate $C'_j(J_1) = \sum_{i \neq j} |a_{ij}|$, $j = 1, \dots, n$. Then, we have

$$\bigcup_{j=1}^{17} \{z \in \mathbb{C} : |z - a_{jj}| \leq C'_j(J_1)\}, \quad (29)$$

where the discs from $j = 1, \dots, 6$, and $j = 10, 11$ locate in the left half plane of \mathbb{C} since $|a_{jj}| > C'_j(J_1)$ for such j . However, the rest of discs may cross the origin and the right half plane of \mathbb{C} . Note that the 17th disc is given by

$$\{z \in \mathbb{C} : |z - (-\frac{d_M + d_F}{2})| \leq b_M + b_F\} \quad (30)$$

which is the disc centered at $-\frac{d_M + d_F}{2}$ with the radius $C'_{17}(J_1) = b_M + b_F$. Since the UAE population is in the increasing trend, i.e. the birth rate is greater than the averaged death rate, we conclude

$$\frac{d_M + d_F}{2} < b_M + b_F. \quad (31)$$

Thus, the 17th disc in (30) surely crosses the origin and the right half plane of \mathbb{C} . Thus, Type I equilibrium point is unstable. By the similar argument, from the jacobian matrix J_2 we can calculate $C'_j(J_1) = \sum_{i \neq j} |a_{ij}|$, $j = 1, \dots, n$. Then, we have

$$\bigcup_{j=1}^{17} \{z \in \mathbb{C} : |z - a_{jj}| \leq C'_j(J_2)\}, \quad (32)$$

where the discs from $j = 1, \dots, 6$, and $j = 10, 11$ locate in the left half plane of \mathbb{C} since $|a_{jj}| > C'_j(J_2)$ for such j . However, the rest of discs may cross the origin and the right half plane of \mathbb{C} . In particular, the 17th disc is given by

$$\{z \in \mathbb{C} : |z - (-\frac{d_M + d_F}{2})| \leq b_M + b_F + \frac{(\eta_M^T \gamma_M G_M^* + \eta_F^T \gamma_F G_F^*) Z_1}{(U^*)^2}\} \quad (33)$$

which is the disc centered at $-\frac{d_M + d_F}{2}$ with the radius

$$C'_{17}(J_2) = b_M + b_F + \frac{(\eta_M^T \gamma_M G_M^* + \eta_F^T \gamma_F G_F^*) Z_1}{(U^*)^2}, \text{ where } Z_1 = \frac{C_{FaddnuM} + C_{MaddnuF}}{N_A^*},$$

$$C_{FaddnuM} = \alpha_M (C_F^{A*} + C_F^{AE*}) \{(1 - \tilde{\nu}_M) C_M^{AE*} + (1 - \nu_M) C_M^{A*}\}, \text{ and}$$

$$C_{MaddnuF} = \alpha_F (C_M^{A*} + C_M^{AE*}) \{(1 - \tilde{\nu}_F) C_F^{AE*} + (1 - \nu_F) C_F^{A*}\}. \text{ Since the population growth of UAE is in the increasing trend, the birth rates are greater than the death rates and hence}$$

$$\frac{d_M + d_F}{2} < b_M + b_F < b_M + b_F + \frac{(\eta_M^T \gamma_M G_M^* + \eta_F^T \gamma_F G_F^*) Z_1}{(U^*)^2} = C'_{17}(J_2). \quad (34)$$

Thus, the 17th disc surely crosses the origin and hence the right half plane of \mathbb{C} . Thus, Type II equilibrium point is unstable. This completes the proof. \blacksquare

Remark In the result in Theorem 2 we observed the 17th disc crosses through the origin from the left half plane to the right half plane of \mathbb{C} from the relation between the birth and death rates of the whole population. Thus, Types I and II equilibrium points are unstable regardless of the premarital screening and education factor. Hence, Types I and II equilibrium points that are our current goal in thalassemia control will not be achievable with the premarital and education factor in a long term.

III. Parameter Estimation

We obtain and estimate the parameter values for the simulations from the 2015 data of the UAE bureau of statistics [2], 2013 Abu Dhabi Statistics Yearbook [3] and 2013 Health Authority of Abh Dhabi [4]. The part of the UAE national population data is summarized in Table 1.

Then, the parameter values are estimated as follows:

- Birth rates: $b_M = \frac{17,279}{476,712} = 0.0362$ and $b_F = \frac{16,761}{476,712} = 0.0352$.

Table 1: The UAE National Census Data

Population (2012)			Birth (2012)			Marriage Contracts (2014)		
M	F	Total	M	F	Total	M	F	Total
231,383	245,329	476,712	17,279	16,761	34,040	9560	8239	17,799

Death rates: $d_M = \frac{1432}{476,712} = 0.0030$ and $d_F = \frac{910}{476,712} = 0.0019$

- Marriage rates:

$$\alpha_M = \frac{\text{Male Marriage Contracts}}{\text{Total Population}} = \frac{9560}{476712} = 0.02$$

$$\alpha_F = \frac{\text{Female Marriage Contracts}}{\text{Total population}} = \frac{8239}{476712} = 0.0172$$

- Screening rates:

$$\alpha_s^M = \frac{\text{Male Marriage Contracts}}{\text{Male total population}} = \frac{9560}{231383} = 0.0413$$

$$\alpha_s^F = \frac{\text{Female Marriage Contracts}}{\text{Female total Population}} = \frac{8239}{245329} = 0.0335$$

- Thalassemia diagnosis adjusting factor: $\eta_M^T = 0.015$ and $\eta_F^T = 0.144$ are chosen such that the proportion of thalassemia major male is less than 0.00025 and the proportion of thalassemia major female is than 0.00024.

References

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